REMARKS

Prior to entry of the present amendment, claims 1, 2, 5-10, 13, 14, and 58-60 are pending. Claims 1, 2, 5-10, 13, 14, and 58-60 are rejected under 35 U.S.C. § 112, first paragraph, and claims 1, 2, 5-10, 13, 14, and 58-60 are rejected under 35 U.S.C. § 103. The specification is objected to. Applicants address each basis for rejection or objection as follows.

Claim amendments

Claims 1, 2, 5-9, and 60 have been amended to recite "an antibody or a functional fragment thereof" and claims 58 and 59 have been amended to recite a "functional" fragment of an antibody. Support for this amendment is found, for example, at page 10, line 16, to page 11, line 10 of the specification (corresponding to paragraphs [0033] and [0034] of the specification published as US 2009/029460).

New claim 61-63 has been added. Support for new claim 61 is found, for example, at page 60, lines 26-31 of the specification (corresponding to paragraph [0178] of the US 2009/029460 publication) and in Figure 17. New claims 62 and 63 find support, for example, at page 60, line 26, to page 61, line 7 of the specification (corresponding to paragraphs [0178] and [0179] of the US 2009/029460 publication) and in Figures 17 and 18 and Example 4 of the specification. No new matter has been added by the present amendment.

Applicants reserve the right to pursue any cancelled subject matter in this or in a continuing application.

Objection to the specification

The specification is objected to for referring to SEQ ID NOS:26 and 27 as polypeptide sequences and SEQ ID NOS:28 and 29 as polynucleotide sequences, whereas the Sequence Listing includes a polynucleotide sequence for SEQ ID NOS:26 and 27 and a polypeptide sequence for SEQ ID NOS:28 and 29. Applicants, herewith, amend the specification correctly identify the sequences. No new matter has been added by the amendment to the specification. This basis for objection may be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 2, 5-10, 13, 14, and 58-60 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Office states (page 2):

> [T]he specification is enabling for an isolated antibody comprising a heavy chain comprising CDR1, CDR2, and CDR3 regions comprising amino acids 28-32, 51-53, and 90-100 of the sequence of SEQ ID NO:29 and a light chain comprising CDR1, CDR2, and CDR3 regions comprising amino acids 11-18, 36-43, and 82-104 of the sequence of SEQ ID NO:28 respectively.

The Office, however, states that the specification is not enabling for "a polypeptide" comprising the above-cited CDR regions because "a polypeptide comprising 6 CDRs does not necessarily require that the CDRs are spacially orientated as in an antibody" (Office Action at page 4), and further states that "it would require undue experimentation to use an antibody that comprises only the 3 heavy chain CDRs or only the 3 light chain CDRs" (Office Action at page 5). Applicants respectfully disagree.

Claim 1, as amended, recites antibody including the human PAM-1 light chain variable region or a functional fragment of such an antibody. With regard to recitation of an antibody including the human PAM-1 light chain variable region, Applicants again direct the Office's attention to Example 2 of the presentation by U.S. Patent and Trademark Office Examiners Yvonne Eyler and Larry Helms entitled "Patenting Antibodies," a copy of which was enclosed with Applicants' last reply. In particular, in Example 2, the following claims are presented:

> Claim 1. An isolated antibody that binds to human antigen X, said antibody comprises a heavy chain variable domain comprising SEQ ID NO:1.
>
> Claim 2. An isolated antibody that binds to human antigen X, said antibody comprises a light chain variable domain comprising SEQ ID NO:2.

The Example further states:

> The instant specification produced an antibody that binds antigen X that contains a VH of SEQ ID NO:1 and a VL of SEQ ID NO:2, as well as explicitly disclosing humanized and chimeric antibodies.
>
> The instant specification provides examples of detection of cancer in human subjects with an antibody that binds antigen X.

And the Example in the presentation notes that there are several prior art references (from 1991 and 1993) that teach methods of producing antibodies that bind a specific antigen by using a specific VL (or VH) and screening a library of complimentary variable domains. In finding sufficient enablement for claims 1 and 2, the Example concludes (emphasis original):

> In light of the prior art disclosing methods of obtaining antibodies that bind an antigen by screening complementary variable domain libraries, the specification's disclosure of an antibody that binds a specific antigen comprising a defined VH or VL sequence would provide enough structure for one skilled in the art to practice the invention.

Applicants submit, as explained below, that the facts of the present case fall squarely within the situation outlined in the above Example of the U.S.P.T.O. presentation and, therefore, the present claims should also be found to be enabled by the specification in view of the state of the art at the time of filing.

Claim 1, as amended, requires the antibody or functional fragment thereof to include a light chain variable region including the sequence of the human PAM-1 antibody (SEQ ID NO:29). Amended claim 1 also requires the antibody or functional fragment thereof to specifically bind to neoplastic cells or cells of a pre-cancerous lesion but not to a normal cell. Claim 2 depends from claim 1 and, as amended, requires the antibody or functional fragment thereof to further include amino acids 11-18, 36-43, and 82-104 of SEQ ID NO:28 (the 3 CDR sequences of the human PAM-1 antibody variable heavy chain) and new claim 61 requires the antibody or functional fragment thereof to also include the human PAM-1 antibody heavy chain variable region having the sequence shown in SEQ ID NO:28. The specification teaches that an antibody containing the sequences of SEQ ID NOS:28 and 29 has the binding specificity required by the claims (see, for instance, Tables 1A and 1B at pages 62 and 63 of the specification).

The specification thus provides the sequence of the variable light and heavy chains of an antibody having the binding properties required by the claims. Consistent with the analysis provided in the U.S.P.T.O.'s presentation, the specification discloses an antibody with the claimed specific binding characteristics, the claims require the antibody or functional fragment thereof to contain at least the variable light chain and, as noted in the U.S.P.T.O. presentation, screening complementary variable domain libraries for antibodies that have the same binding

characteristics was standard in the art at the time of filing. Applicants submit that the claims provide sufficient structure for one skilled in the art to make and use the invention within the full scope of the claims as amended. This basis for rejection may be withdrawn.

With respect to claim 2, Applicants note that this claim, as amended, requires the antibody or functional fragment thereof to include the three CDR sequences of both the variable heavy and light chain sequences of the PAM-1 antibody described in the specification. As such, the antibody or functional fragment thereof of claim 2, as amended, contains all 6 CDRs of the PAM-1 antibody.

Applicants further submit that new claims 61 and 62, which is directed to an antibody or functional fragment thereof containing both the variable light chain and variable heavy chain sequences of the PAM-1 antibody (i.e., including the sequences of SEQ ID NOS:28 and 29), and new claim 63 which is directed to an antibody or functional fragment containing the 6 CDR regions of the human PAM-1 antibody, are also free of this basis for rejection because these claims are directed to embodiments that the Office has indicated to be enabled by the specification as filed.

Applicants also submit that recitation of a "functional" fragment of an antibody in the claims, as amended, overcomes the Office's objection to recitation of antibody "fragments" because the "term fragment is interpreted to mean an antibody fragment that does not comprise all 6 CDRs" (Office Action at page 5).

A functional fragment is defined in the specification at page 10, lines 16-21 (corresponding to paragraph [0033] of the US 2009/0029460 publication) to be a fragment that retains a biological activity of the full length antibody such as ability to specifically bind an antigen, induce apoptosis and/or inhibit cell proliferation. The specification, at page 10, line 22, to page 11, line 10 (corresponding to paragraph [0034] of the US 2009/0029460 publication), provides V_L, V_H, Fab, Fab' and $F(ab')_2$ fragments as examples of "functional fragments." A skilled person would know how to generate functional fragments such as these and would know how to determine whether the fragment retains the biological activity of the full-length antibody using, for instance, the binding assays described in the Examples of the present specification. Applicants submit that, in view of the teachings in the specification and the knowledge in the art,

the skilled worker would know how to make and use the functional fragments of an antibody encompassed by the claims.

For all the above reasons, Applicants submit that the claims as amended are free of the scope of enablement rejection set forth in the current Office Action. Reconsideration and withdrawal of this basis for rejection is respectfully requested.

Rejection under 35 U.S.C. § 103

Claims 1, 2, 5-10, 13, 14, and 58-60 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Vollmers et al. (Cancer 74:1525-1532, 1994; "Vollmers"), as evidenced by Brändlein et al. (Human Antibodies 11:107-119, 2002; "Brändlein"), in view of Robinson et al. (U.S. Patent No. 5,618,920; "Robinson"). Applicants, for the reasons explained below, submit that this basis for rejection should be withdrawn.

The Office, in essence, maintains that the skilled person would be motivated to produce a recombinant PAM-1 antibody because PAM-1 binds to cancer cells, and the recombinant PAM-1 antibody would necessarily induce apoptosis of cancer cells (Office Action at pages 5-9). Applicants disagree with this line of reasoning because, as stated in the last reply, the cited prior art teaches that the PAM-1 antibody induces *proliferation* of cancer cells, so there would be no motivation to produce a recombinant version thereof. Nonetheless, Applicants note that the Office, at page 9, states:

> [T]his rejection is based on the assumption that the antibody PAM-1 was publicly available to enable one of skill in the art to make a genetically engineered antibody comprising the sequences of SEQ ID NO:28 and SEQ ID NO:29. If the PAM-1 antibody was in sole possession of the Applicants up to the filing date of the present application, an affidavit to that effect would obviate this rejection.

Applicants, herewith, submit a Declaration by inventor Dr. Frank Hensel. Dr. Hensel states (paragraph 3):

> The PAM-1 antibody described in the above-identified patent application, which includes the amino acid sequences of SEQ ID NOS:28 and 29, and is encompassed by the pending claims, was not publicly available before the January 26, 2004 filing date of U.S. application serial no. 10/764,730, from which the present application claims benefit.

Applicants submit that, in view of Dr. Hensel's Declaration that the PAM-1 antibody was not publicly available before the priority date of the present application, the obviousness rejection over Vollmers, as evidenced by Brändlein, and in view of Robinson may be withdrawn.

CONCLUSION

Applicants submit that the application is now in condition for allowance, and such action is hereby respectfully requested.

Enclosed is an authorization to charge $220 to Deposit Account No. 03-2095 for the addition of two independent claims in excess of three.

Enclosed is a Petition to extend the period for replying to the Office Action for one (1) month, to and including April 7, 2011, and an authorization to charge the required extension fee to Deposit Account No. 03-2095.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Kristina Bieker-Brady, Ph.D.
Reg. No. 39,109

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045